REMARKS

Reconsideration of this application is respectfully requested.

I. Formal Matters

Applicants acknowledge that the Examiner for this application is now Stacy Brown Chen.

II. Status of the Claims

With entry of this amendment, claims 56-61 and 73-87 are pending. Applicants cancel withdrawn claims 1-55 and 62-72 without surrender or disclaimer of the subject matter recited therein. Applicants note that the Office Action Summary states that claims 1-54 and 62-71 are withdrawn from consideration, but the body of the Office Action (page 2) states that claims 1-55 and 62-71 are withdrawn, and that claims 56-61 are under consideration. Applicants believe the latter statement is correct.

Applicants have amended claims 56 and 57 to provide greater precision to the claim language. Applicants also present new claims 73-87. Support for these claims can be found in, for instance, in Example 1, beginning on page 38, in paragraph [057], and in paragraph [0157]. No new matter is presented.

III. Claim Objections

The Office objects to claims 56-61 "for a minor informality." Office Action, p. 2 The Office states that "[i]n the method steps of claims 56 and 57, the cells are not specified as being dendritic cells, although the last paragraph of both claims indicates that dendritic cells are essential to the assay." *Id.*

Applicants respectfully submit that neither claim 56 nor claim 57 indicate that the dendritic cells "are essential to the assay" as alleged by the Office. Moreover,

dependent claim 58 recites dendritic cells (DC), indicating that the claims from which it depends include more than dendritic cells. Accordingly, Applicants have amended claims 56 and 57 to recite "the cells."

IV. Objection to the Specification

The Office objects to the specification as allegedly "failing to provide antecedent basis for the claimed subject matter" of claim 56, and cites 37 C.F.R. § 1.75(d)(1) and M.P.E.P. § 608.01(o). Office Action, p. 2. The Office alleges that "[t]he specification discloses 95% inhibition in paragraph [0109], but not 95% modulation, which encompasses more than inhibition activity." *Id.* The Office apparently refers to paragraph [0109] of the published application, rather than the specification as-filed.

Applicants respectfully traverse. As explained in M.P.E.P. § 608.01(o), 37 C.F.R. § 1.75(d)(1) is designed to prevent Applicants from amending the claims to recite subject matter in a confusing manner:

> Usually the terminology of the original claims follows the nomenclature of the specification, but sometimes in **amending the claims or in adding new claims**, new terms are introduced that do not appear in the specification. The use of a confusing variety of terms for the same thing should not be permitted.
>
> Note that examiners should ensure that the terms and phrases used in claims presented **late in prosecution** of the application (including claims amended via an examiner's amendment) find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description, see 37 CFR 1.75(d)(1). If the examiner determines that the claims presented **late in prosecution** do not comply with 37 CFR 1.75(d)(1), applicant will be required to make appropriate amendment to the description to provide clear support or antecedent basis for the terms appearing in the claims provided no new matter is introduced.

M.P.E.P. § 608.01(o) (emphasis added). Applicants respectfully submit that claim 56 is an original claim, not one added late in prosecution and that 37 C.F.R. § 1.75(d)(1) is not relevant to that claim. Applicants respectfully request that the Office withdraw the objection.

V. The Claims Are Definite

The Office rejects claims 56-61 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Office Action, p. 4. The Office asserts that "[l]acking a clear definition of the units for measurement of these binding values, the metes and bounds of the claims cannot be determined." *Id.*

Applicants respectfully traverse. The inquiry under 35 U.S.C. § 112, second paragraph, is whether the claims apprise the skilled artisan of their scope. *See* M.P.E.P. § 2173.02. Applicants respectfully submit that units of measurement need not be recited in the claims. As indicated by the Office on page 3 of the Office Action, one way to envision the claimed subject matter is in the form of an equation, as set forth on that page. As can be seen from the equation, the binding value in the presence of test substance is divided by the baseline binding value. Accordingly, the result is a number without units (a ratio).

Applicants respectfully submit that one of skill in the art would understand the claimed methods involve measuring the ratio between the two values to produce a value without units, and would know the claims' scope. In claims 56 and 57, that ratio is discussed as a percentage (95% modulation and 95% inhibition, respectively). Similarly the specification states:

> "Inhibition" is measured by comparing the extent of effector molecule binding to DC-SIGN in the presence of a DC-SIGN blocker with the extent of effector molecule binding to DC-SIGN in the absence of a DC-SIGN blocker. The ratio of extent of binding in the presence of the DC-SIGN blocker compared to the extent of binding in the absence of the DC-SING blocker is then determined. The percent inhibition is then the proportional reduction in the amount of binding. For example, a **ratio** of 0.1 represents a 90% reduction in binding.

Specification, paragraph [0110] (emphasis added).

In view of the common knowledge that a ratio does not have units, combined with the description in the specification, Applicants respectfully submit that claims 56-61 are definite and respectfully request that the Office withdraw the rejection.

The Office also rejects claims 56-61 on the grounds that the claims recite a DC-SIGN receptor, which the specification defines as DC-SIGN and/or DC-SIGNR or homologues of a DC-SIGN receptor. Office Action, p. 4. According to the Office, "[a]pplicant has not defined the homologues' structures such that the metes and bounds of the homologues can be determined." *Id.* at 4-5.

Applicants respectfully traverse. Under 35 U.S.C. § 112, second paragraph, the claims need only "set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity." M.P.E.P. § 2173.02. (emphasis added). As stated by the Federal Circuit, "[o]nly when a claim remains insolubly ambiguous without a discernible meaning after all reasonable attempts at construction must a court declare it indefinite." *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1366 (Fed. Cir. 2004). Here, the specification directs the reader to Curtis *et al.*, "Sequence and expression of a membrane-associated C-type lectin that exhibits CD4-independent

binding of human immunodeficiency virus envelope glycoprotein gp120," Proc. Natl. Acad. Sci. 89: 8356-60 (1990) ("Curtis"), which discloses the sequence of human DC-SIGN. Applicants enclose a copy of Curtis. The specification also directs the reader to Pöhlmann *et al.*, "DC-SIGNR, a DC-SIGN homologue expressed in endothelial cells, binds to human and simian immunodeficiency viruses and activates infection in trans," Proc. Natl. Acad. Sci. 98: 2670-75 (2001) ("Pöhlmann"), which describes the sequence of DC-SIGNR. The Office cited Pöhlmann in the Restriction Requirement mailed April 2, 2008, and a copy of Pöhlmann is not enclosed. In addition to disclosing the sequence of DC-SIGNR, Pöhlmann states that "DC-SIGN and DC-SIGNR share 77% amino acid identity," and identifies the C-type lectin domain and neck regions as "the greatest areas of homology." Pöhlmann, p. 2671, col. 2, under the heading "DC-SIGNR Protein is Expressed on Endothelial Cells in Placenta, Lever and Lymph Nodes." Applicants respectfully submit that the specification directs the skilled artisan to the sequences of DC-SIGN and DC-SIGNR, describes the similarity between those sequences, and identifies regions that would be expected to be conserved in additional homologs. From this description, one of skill in the art could clearly envision the metes and bounds of the claims. Accordingly, Applicants respectfully request that the Office withdraw the rejection.

VI. The Claims Are Enabled

The Office rejects claims 56-60 for alleged failure to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph. Office Action, p. 5. The Office admits that the specification "is enabling for a method of identifying a DC-SIGN blocker, wherein the viral effector molecule is gE of Dengue virus and the DC-SIGN receptor is

DC-SIGN (not homologues thereof)." *Id.* Applicants understand gE to mean "E glycoprotein" as recited in the claims. However, the Office asserts that the specification "does not reasonably provide enablement for a method of identifying a DC-SIGN modulator, wherein the viral effector molecule is a non-gE of Dengue virus and the DC-SIGN receptor is a DC-SIGN homolog." *Id.*

In support of its allegation of lack of enablement, the Office states that "the claims encompass a method of identifying a DC-SIGN modulator," but "the definition of DC-SIGN is not clear because it encompasses homologues of both DC -SIGN, DC-SIGNR, and homologues of homologues." Office Action, p. 6.

The Office also asserts that the state of the art shows that "DC-SIGN mediates Dengue virus infection, specifically THP-1 cells," and also confirms that "DC-SIGN binds Human Cytomegalovirus (envelope protein B) and HIV gp120." *Id.* However, the Office asserts that "[t]here are no other Dengue virus molecules identified in the specification as capable of interacting with DC-SIGN," and that "the specification does not provide guidance for identifying DC-SIGN and DC-SIGNR homologues, or homologues of homologues." *Id.* According to the Office, "given the breadth of the claims, the state of the art, and the limited guidance and working examples in the specification, it would require undue experimentation to practice the claimed method in its full breadth." *Id.*

Applicants respectfully traverse. The Office appears to rely on some of the factors identified in *In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) as relevant to enablement. Applicant discusses these factors below.

A. Scope of the Claims

Applicants respectfully submit that the breath of the claims is not uncertain. As discussed above, the skilled artisan could readily envision the metes and bounds of the claimed methods

B. State of the Art and Examples

Applicants respectfully submit that the state of the art, when combined with disclosure in the specification, supports enablement of the claims. The Office highlights several known examples of the relationship between DC-SIGN, and multiple viruses, including Dengue, human cytomegalovirus, and HIV. Applicants respectfully submit that the known relationship between DC-SIGN and multiple viruses, when combined with the disclosure of the specification, indicates that one of skill in the art would expect multiples viruses to interact with DC-SIGN in the claimed methods.

Moreover, Applicants respectfully submit that the application enables the claimed method using molecules other than those from Dengue virus. First, as described above, multiple viruses interact with DC-SIGN, and one of skill in the art could practice the claimed method with the molecules from those viruses that interact with DC-SIGN. Second, the specification discloses the use of molecules from multiple flaviviruses, including Dengue, West Nile virus, and Yellow Fever (Example 1), and reports that DC-SIGN mediates entry of Dengue and West Nile virus, but not Yellow Fever (Example 9). Third, the specification discloses methods for investigating the interaction of DC-SIGN with viral proteins (Example 4), methods for detecting viral infection (Example 5),

methods for examining the ability of a monoclonal antibody to block DEN-1 infection (Example 8) and a variety of additional blocking molecules (Example 9).

Applicants respectfully submit that one of skill in the art could make and test various viral molecules for their ability to interact with DC-SIGN. When combined with high-throughput screening methods, such as protein arrays, one of skill in the art could rapidly identify molecules that bind DC-SIGN and could be used in the claimed methods. *See, e.g.*, Ng and Ilag, "Biomedical Applications of Protein Chips," J. Cell. Mol. Med. 6: 329-40 (2002), a copy of which is enclosed for the Examiner.

C. Guidance

Applicants respectfully submit that, when combined with the knowledge in the art, the specification provides sufficient guidance to enable the skilled artisan to practice the claimed methods using DC-SIGN, DC-SIGNR and homologues of those proteins. As described above, the specification cites publications that provide the sequence of DC-SIGN and DC-SIGNR. In addition, as noted above, Pöhlmann describes the domains of DC-SIGN and DC-SIGNR that are conserved. Specifically, Pöhlmann identifies the C-type lectin domain as one of the areas of greatest homology. Curtis, provides an alignment of the lectin domain of multiple proteins, a technique by which the skilled artisan could identify DC-SIGN homologues. Curtis, p. 8359, Figure 3. As described in detail above, the specification directs the reader to Pöhlmann and Curtis, and provides substantial guidance by which the skilled artisan could examine the interaction between the DC-SIGN homologs and a variety of molecules known to interact with DC-SIGN.

Applicants respectfully submit that claims 56-60 are fully enabled and request that the Office withdraw the rejection.

VII. The Claims Are Not Obvious

A. Figdor

The Office rejects claims 56-58 under 35 U.S.C. § 103(a) as allegedly being unpatentable over International Application Publication No. WO 00/63251 ("Figdor"). Office Action, p. 7. According to the Office, Figdor "discloses the identification of a compound that binds to DC-SIGN on dendritic cells ('a C-type lectin') for modulating the interaction, particularly, reducing the interaction." *Id.* The Office also alleges that Figdor discloses "the determination of antibodies that bind to DC-SIGN on dendritic cells, and the determination that those antibodies can reduce HIV infectivity of dendritic cells," and cites Example 8. *Id.* The Office admits "the specific method steps of determining baseline values are not explicitly set forth in Figdor's disclosure," but asserts that "the basic steps are disclosed." *Id.* The Office concludes that "it would have been well within the ability of the ordinary artisan to select a value (a percentage, for example) that represents significant modulation of DC-SIGN activity." *Id.*

Applicants respectfully traverse. Obviousness cannot be based on a conclusory statement, rather "[t]here must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *Innogenetics v. Abbott Labs.*, 512 F.3d 1363, 1373 (Fed. Cir. 2008). Here, the Office admits that "the specific method steps of determining baseline values are not explicitly set forth in Figdor's disclosure," but provides no reason why one of skill in the art would modify Figdor's disclosure to include the process of determining a baseline binding value, determining a

binding value in the presence of a test substance and determining a test substance binding modulation value for the test substance as recited in claims 56 and 57. Applicants respectfully submit that the Office has not established *prima facie* obviousness because it has failed to provide any reason why one of skill in the art would have modified Figdor to arrive at the claimed invention. Applicants respectfully request that the Office withdraw the rejection.

B. Figdor and Banka

The Office rejects claims 59 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Figdor "as applied to claim 57 above" and further in view of Banka *et al.* "THP-1 cells form foam cells in response to coculture with lipoproteins but not platelets," J. Lipid Research, 32: 35-43 (1991) ("Banka"). Office Action, pp. 7-8. The Office admits that "Figdor does not disclose THP-1 dendritic cells, although Figdor does disclose the derivation of DCs from monocytes." *Id.* However, the Office asserts that "it would have been obvious to select a cell line like THP-1 for an assay that requires continuous expression of DC-SIGN because the THP-1 cell line is expected to produce dendritic cells that express DC-SIGN.

Applicants respectfully traverse. As discussed above, the Office has provided no rationale why one of skill in the art would have modified Figdor. Moreover, the Office cites Banka, but does not state what Banka allegedly teaches or if it is relevant to the alleged obviousness of the claims. Accordingly, Applicants respectfully submit that the Office has failed to establish *prima facie* obviousness of claim 59 because the Office

has not provided any rationale for why one of skill in the art would have modified Figdor, and had not provided any information about the purported relevance of Banka.

Applicants respectfully request that the Office withdraw the rejection.

VIII. Conclusion

In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration of this application and the timely allowance of the pending claims.

If there is any fee due in connection with the filing of this Response, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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